REMARKS

In the Office Action, previous claims 1-41 have been renumbered 1-40 due to no claim 28 being presented. In the present Amendment, the Applicants have noted that the claim numbers used in this Office Action reflect the renumbering of the claims.

Claims 1-14, 17-19, 25, 29 and 38-40 were rejected, and claims 15, 16, 20, 24, 26-28 and 30-37 were objected to.

As can be seen from above in the present Amendment, claims 2-7 and 24-29 have been canceled, and claims 1, 17, 20, 35 and 38-40 have been amended. Claims 24-29 have been canceled to be consistent with the cancellation of claims 2-7. Claim 20 has been amended to be consistent with the amendment of claim 1. Claims 1, 8-23 and 30-40 are now pending in this application. Claims 1, 17, 20 and 39 are independent claims. The amendments to the pending claims are supported in the specification and claims. No new matter has been added.

Independent claims 1 and 20 have been amended to include the additional limitation, which was respectively contained in canceled claims 2 and 24 and described in the Specification, that the enzyme source "is selected from the group consisting of cell-free extract, partially purified enzyme, and purified enzyme." Support for this additional limitation can be found, for example, in original claims 2 and 24, on page 10, lines 1-5 and page 15, lines 11-15 of the Specification, and in Examples 2-9 on pages 32-46 of the Specification. Claims 1 and 20 have also been amended to correct clerical errors and to clarify steps b) and c) for claim 1 and steps c) and d) for claim 20.

Claims 17 and 39 have been amended, as proposed by the Examiner, to stand on their own as independent claims by amending the preamble to be directed to "A process for producing a derivatized compound of para-hydroxystyrene comprising," and by incorporating the steps of amended claims 1 and 20, respectively.

Claim 38 has been amended to correct a clerical error.

Claims 35 and 40 have been amended to correct dependency to claims 34 and 39, respectively.

Objections

Claims 15, 16, 20, 24, 26-28 and 30-37 were objected to (as indicated by box 7 or PTOL-326) of the Office Action. Since the Office Action did not further disclose the specifics or details of the objections, the Applicants were not able to address nor respond to the objections.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 7, 17-19, 25, 29 and 38-40 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-7 and 24-29 have been canceled, and thus the rejections directed to claims 7, 25 and 29 are rendered moot.

In the Office Action, the Examiner asserts that claims 17-19 and 39-40 are drawn to a process for producing a derivative of para-hydroxystyrene. As proposed by the Examiner, claims 17 and 39 have been amended to stand on their own as independent claims by amending the preamble to be directed to "A process for producing a derivatized compound of para-hydroxystyrene comprising," and by incorporating the steps of claims 1 and 20, respectively. Claims 18 and 19 depend from claim 17, and claim 40 depends from claim 39.

Further, the Examiner asserts that claim 38 is indefinite in the recitation of "wherein the fermentation medium after step (c) is optionally added back to the biphasic reaction medium." Claim 38 has been amended to no longer recite the indefinite language.

Accordingly, the Applicants respectfully request withdrawal of the 35 U.S.C. § 112, second paragraph, rejections directed to claims 17-19 and 38-40.

Rejections Under 35 U.S.C. §103(a)

The Applicants confirm that the subject matter of the claimed invention were commonly owned at the time the claimed invention was made and is commonly owned at the present time.

Claims 1-3 and 8-14 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cavin et al. (Applied and Environmental Microbiology 64(4):1466-1471, 1998) in view of Lee et al. (Enzyme and Microbial technology 23:261-266, 1998). Claims 2 and 3 have been canceled, and thus the rejections directed to claims 2 and 3 are rendered moot. The Applicants respectfully traverse the rejections directed to claims 1 and 8-14 for the reasons set forth below.

In the Office Action, the Examiner asserts that Cavin et al. "teach the purification and characterization of the *B. subtilis* decarboxylase of SEQ ID NO:4 of the instant application," and also "teach that the decarboxylase of SEQ ID NO:4 uses p-coumaric acid (also known as para-hydroxycinnamic acid), ferulic acid and caffeic acid as substrates ..." The Examiner also asserts that decarboxylation of p-coumaric acid would produce para-hydroxystyrene. Further, the Examiner asserts that Cavin et al. "uses *B. subtilis* crude cell extracts for enzymatic characterization of the enzyme (Table 1)." In addition, the Examiner admits that Cavin et al. "does not teach production of para-hydroxystyrene in a biphasic medium."

With regard to the Lee et al. reference, the Examiner asserts that Lee et al. "teach decarboxylation of ferulic acid to 4-vinylguaiacol by whole cells of *B. pumilus* that produce a ferulate decarboxylate in an aqueous/organic solvent two-phase system (Abstract)." The Examiner also asserts that Lee et al. "also teach the partition coefficient of ferulic acid and 4-vinylguaiacol in various solvents including hexane (Table 1), the enzymatic activity of the decarboxylase contained in whole *B. pumilus* cells using different solvents including hexane (Table 2), ..." Further, the Examiner asserts that Lee et al. "teach that the best results were obtained with a two-phase system containing equal volumes (50%/50%) of hexane and phosphate buffer (page 264, left column, second full paragraph)." In addition, the Examiner admits that Lee et al. "do not teach the production of para-hydroxystyrene or the decarboxylase of SEQ ID NO:4."

The Examiner claims that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to produce para-hydroxystyrene, which is a derivative of 4-vinylguaiacol, using the method described by Lee et al., wherein the enzyme source is immobilized and/or the enzyme source is recovered by centrifugation or filtration, and wherein para-hydroxystyrene is recovered by adsorption by resins (e.g., HPLC). A person of ordinary skill in the art is motivated to produce para-hydroxystyrene in a biphasic medium for the benefit of avoiding substrate and product inhibition, as taught by Lee et al. with regard to a similar decarboxylase from *B. pumilus* (page 262, left column, lines 2-3, first full paragraph). In the absence of evidence to the contrary, one of skill in the art would expect the decarboxylase of Cavin et al. to also experience substrate and product inhibition. Also, one of skill in the art is motivated to immobilize the enzyme source as immobilization allows for recovery of the enzyme, lower operation costs as enzyme loss is less likely, and potential enzyme stability ... One of ordinary skill in the art has a reasonable expectation of success at producing para-hydroxystyrene using the method described by Lee et al. for 4-vinylguaiacol with the enzyme of Cavin et al. and para-hydroxycinnamic acid as the substrate in view of the fact that Cavin discloses the enzyme which catalyzes the decarboxylation of para-hydroxycinnamic acid and Lee et al. teach the successful use of a biphasic medium with hexane for 4-vinylguaiacol, which is a structurally close derivative of para-hydroxystyrene ... Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made."

The Examiner has correctly cited Cavin et al. as teaching the purification and characterization of the *B. subtilis* decarboxylase of SEQ ID NO:4 of the instant application, and that the decarboxylase of SEQ ID NO:4 uses p-coumaric acid (also known as para-hydroxycinnamic acid), ferulic acid and caffeic acid as substrates. Further, the Examiner is correct in stating that Cavin et al. do not teach production of para-hydroxystyrene in a biphasic medium.

The Examiner has correctly cited Lee et al. as teaching decarboxylation of ferulic acid to 4-vinylguaiacol by whole cells of *B. pumilus* that produce a ferulate decarboxylate in an aqueous/organic solvent two-phase system. In addition, the Examiner is correct in stating that Lee et al. do not teach the production of para-hydroxystyrene or the decarboxylase of SEQ ID NO:4.

It is axiomatic that in order to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, in the references or in the general knowledge of the art, to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all the claim limitations. The Applicants submit that a prima facie has not been met.

In the instant application, independent claim 1 has been amended to include the additional limitation, which was contained in canceled claim 2 and described in the Specification, that the enzyme source "is selected from the group consisting of cell-free extract, partially purified enzyme, and purified enzyme." Support for this additional limitation can be found, for example, in original claim 2, on page 10, lines 1-5 and page 15, lines 11-15 of the Specification, and in Examples 2-9 on pages 32-46 of the Specification.

The Applicants respectfully assert that Lee et al. explicitly use whole cells and do not contemplate use of cell-free extract nor partially purified enzyme nor purified enzyme in a process for producing 4-vinylguaiacol from the decarboxylation of ferulic acid. Further, the Applicants respectfully assert that Lee et al. teach away from the use of cell-free extracts or purified enzyme by their statement on page p. 263 (last sentence of first full paragraph in the Results and discussion section): "Because purified ferulate decarboxylase is subject to both substrate and product inhibition, and styrene toxicities are well known in the biological systems, we sought to develop a two-phase, aqueous-organic reaction system which might successfully remove product and enhance vinylguaiacol synthesis."

Since Lee et al. do not teach the production of para-hydroxystyrene or the decarboxylase of SEQ ID NO:4 and teach away from the use of cell-free extracts or purified enzyme and Cavin et al. do not teach production of para-hydroxystyrene in a biphasic medium, the Applicants submit that there is no motivation in either of the cited references to combine the teachings. In addition, the Applicants have unexpectedly discovered that a higher yield of para-hydroxystyrene was achieved through the use of an enzyme source having para-hydroxycinnamic acid decarboxylase activity wherein the enzyme source is selected from the group consisting of cell-free extract, partially purified enzyme, and purified enzyme. The Applicants respectfully assert that this unexpected discovery goes against conventional wisdom to one of ordinary skill in the art, who would expect that a whole cell catalyst would be better suited and more stable for the claimed invention.

In view of the above arguments, the Applicants submit that currently amended claim 1 and also claims 8-14, each of which depends from claim 1, are not obvious and comply with

all the elements of 35 U.S.C. § 103(a). Accordingly, the Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejections directed to claims 1 and 8-14.

Double Patenting Rejections

Claims 1-2 and 4-14 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14, 17-19 of copending Application No. 10/439,478 ('478 Application) in view of Lee et al. Applicants traverse.

Claims 2 and 4-7 have been canceled, and thus the rejections directed to claims 2 and 4-7 are rendered moot. While not intending to agree with the examiner's reasoning with respect to this nonstatutory obviousness-type double patenting rejection, Applicants file herewith a terminal disclaimer disclaiming the terminal part of any patent that grants on the instant application that extends beyond the term of Application No. 10/439,478.

In view of the filing of the terminal disclaimer applicants submit this rejection is moot.

CONCLUSIONS

In view of the amendments and remarks presented above, the Applicants submit that pending claims 1, 8-23 and 30-40 are patentable over the art of record, and that this case is otherwise in condition for allowance.

Should the Examiner wish to discuss any issues involved in this application, the Examiner is respectfully invited to contact the undersigned at the telephone exchange set forth below.

Should there be any fee due in connection with the filing of this Amendment, please charge such fee to Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company).

Respectfully submitted,

/S. NEIL FELTHAM/
S. NEIL FELTHAM
ATTORNEY FOR APPLICANTS
Registration No.: 36,506
Telephone: (302) 992-6460
Facsimile: (302) 992-5374

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